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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/974,186	11/18/97	BOYLE W	A-378D5

HM22/0428

U.S. PATENT DEPARTMENT/RBW
AMGEN, INC
AMGEN CENTER, M/S 10-1-B
1840 DE HAVILLAND DRIVE
THOUSAND OAKS CA 91320-1789

EXAMINER	
CAMPELL, B	
ART UNIT	**PAPER NUMBER**
1632	14

DATE MAILED: 04/28/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
8/974,186	Boyle et al
Examiner	**Group Art Unit**
Campell	1632

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 3/14/00.

☑ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 49-53 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 49-53 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

The amendment filed March 14 has been entered.

Claim Objections

Claims 52 and 53 fail to comply with the sequence rules because they do not recite a SEQ ID No., as previously stated (paper 12, p. 2). Compliance with the sequence rules is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, as previously stated (paper 4, pp. 2-4; paper 8, p. 2; paper 12, pp. 2-4).

Applicants argue that the claimed method is not intended to be limited to any particular purpose. This argument is not persuasive. Claims 51-53 explicitly state that the method is performed in humans. It is difficult to imagine why this would be done for any purpose other than gene therapy. Furthermore, Applicants' reliance on *Intervet America, Inc. v. Kee-Vet Laboratories* is misplaced because that case dealt with limitations read into the claims from attorney's arguments, not the specification. Applicants argue that the methods could be used for other purposes, but this argument is not persuasive because the specification does not indicate any other purposes. Production of osteoprotegerin in a transgenic animal does not appear to be the object of the claimed methods, since the claims do not recite production of a transgenic animal or recovery of the protein. (Claims drawn to isolation of the protein from a transgenic animal might be allowable, however, if adequately supported in the specification.)

Applicants argue that the Examiner has not explained why one would not be able to "extrapolate" the disclosed transgenic animals into a gene therapy method. The Examiner agrees that the disclosure suggests that therapeutic methods using osteoprotegerin protein or nucleic acids could eventually be

developed. However, the specification does not enable the skilled artisan to develop a gene therapy method without undue experimentation. The state of the prior art as of 1995 was that gene therapy was not routinely successful. The claims are broad, since there are virtually no limitations to the claimed methods. There is no working example. The predictability of the art is low, not only because it is "physiological," but also because there is no evidence of similar proteins being expressed to effect a therapeutic treatment. Most important, the specification provides virtually no guidance regarding how to practice a gene therapy method. Applicants are reminded that, "Tossing out the mere germ of an idea does not constitute enabling disclosure....It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." See *Genentech v. Novo Nordisk A/S*, 42 USPQ2d 1001, at p. 1005. All of the "*Wands* factors" discussed above weigh against Applicants. A *prima facie* case of non-enablement has been established.

Applicants argue that therapy by an antisense method is enabled. This argument is not persuasive for the reasons discussed above and in the previous Office action. Applicants argue that Example 3 enables the invention. Example 3 describes the production of transgenic mice. If Applicants wish to claim a method of making transgenic animals which express OPG, such claims would probably be allowable (if commensurate in scope with the claims issued in patent no. 6,015,938). However, the claims in their present form do not appear to recite methods for making transgenic animals.

Applicants argue that they are puzzled as to how antisense therapy can not be enabled when it apparently works. On the other hand, the Examiner is puzzled as to why no antisense drugs are on the market if they are so effective. Apparently the antisense therapies having progressed to clinical trials were not successful. In fact, the first antisense drug was approved for clinical use in 1998 (3 years after Applicants' effective filing date). Furthermore, this drug was approved for treatment of viral infections of the eye, wherein the antisense oligo is injected directly into the ocular fluid. Thus the effectiveness of the treatment results from the unique treatment method, which circumvents most of the delivery and stability problems which are described in the previously cited references. Applicants argue that the teachings of the

specification combined with routine experimentation would enable the claimed methods. What teachings in the specification?

In conclusion, a *prima facie* case of non-enablement has been established, and Applicants have not rebutted the *prima facie* case with evidence. Argument alone is not sufficient when evidence is required. See *In re Schulze*, 145 USPQ 716.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce Campell, whose telephone number is 703-308-4205. The examiner can normally be reached on Monday-Thursday from 8:00 to 4:30 (Eastern time). The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached on 703-308-2035. The FAX phone numbers for group 1600 are 703-308-4242 and 703-305-3014.

An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

BRUCE R. CAMPELL
PRIMARY EXAMINER
TECHNOLOGY CENTER 1600